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10/069,236	02/22/2002	Hadar Kless	02/23375	1424

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EXAMINER

WILDER, CYNTHIA B

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 08/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/069,236

Applicant(s)

KLESS, HADAR

Examiner

Cynthia B. Wilder, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12,16 and 19 is/are pending in the application.
- 4a) Of the above claim(s) 1-11,13-15,17,18 and 20-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12,16 and 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 9/25/2002.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 12, 16 and 19 in the reply filed on May 20, 2004 is acknowledged. Accordingly, claims 1-11, 13-15, 17-18, and 20-32 have been withdrawn from consideration as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of extending a nascent oligonucleotide-3'-OH in a template dependent manner, the method comprising the step of contacting the nascent oligonucleotide with a nucleic acid template, a template dependent polymerase and 1^N to 4^N oligonucleotide triphosphates each including N monomer, wherein N is an integer of 2 or 3, it does not reasonably provide enablement for a method of extending a nascent oligonucleotide-3'-OH in a template dependent manner, the method comprising the step of contacting the nascent oligonucleotide with a nucleic acid template, a template dependent polymerase and 4^N oligonucleotide triphosphates, each including N monomers, wherein N is any integer greater than one. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with

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these claims. The first paragraph of section 112 requires the specification describe how to make and use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue (See *In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988)). These factors include, but are not limited to:

I. Quantity of Experimentation Necessary:

The claimed invention is drawn to a method of extending a nascent oligonucleotide-3'-OH in a template dependent manner, the method comprising the step of contacting the nascent oligonucleotide 3'-OH with a nucleic acid template, a template dependent polymerase and 4^N oligonucleotide triphosphates, each including N monomers, wherein N is an integer greater than 1, under conditions in which said nascent oligonucleotide-3'-OH hybridizes with said nucleic acid template and said template-dependent polymerase is active in incorporating said oligonucleotide triphosphate onto a growing 3'-OH group of the nascent oligonucleotide-3'-OH, thereby extending the nascent oligonucleotide 3'-OH in a template dependent manner. At page 18 of the specification, Applicant describes that a plurality of oligonucleotides triphosphates is provided comprising 4^N oligonucleotide triphosphates, each having N monomers in a single mix or any combination of submixes, wherein N is an integer greater than 1. The specification teaches that thus, "if N equals 2 (dinucleotide), 16 different oligonucleotide triphosphates are included in the single mix or any combination of the submixes; if N equals 3 (trinucleotide), 64 different oligonucleotide triphosphates are included in the single mix or any combination of the sub-mixes; if N equals 4 (tetranucleotide), 256 different oligonucleotide triphosphates are included in the single mix or any combination of the sub-mixes; if N equals 5 (pentanucleotide,

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1024 different oligonucleotides triphosphates are included in the single mix or any combination of the sub-mixes; whereas if N equals 6 (hexanucleotide), 4096 different oligonucleotide triphosphates are included in the single mix or any combination of the sub-mixes, and so on". Despite extensive statements in the specification referring to 4^N oligonucleotide triphosphates, wherein N is any monomer greater than 1, there is no enabling disclosure as to the incorporation of oligonucleotide triphosphates onto a nascent oligonucleotide-3'OH in a template dependent manner comprising 4^N wherein N is *greater than 2* or 3 monomers (dinucleotide or trinucleotide) as claimed. Likewise, there is no indication from the claims or specification that an oligonucleotide triphosphate comprising four or five or six or even ten or twelve monomers is capable of being incorporated by template-dependent polymerization. No information is provided that would enable one of ordinary skill in the art to make or use oligonucleotide triphosphates of any length and composition with any template-dependent polymerase without undue experimentation. Neither the Detailed Description of the invention or the Examples provided teach pertinent information concerning conditions necessary for an oligonucleotide triphosphate comprising any number of monomers to function in the method as claimed. In fact, the examples, especially Example 7 provides only a limited teaching wherein dinucleotides and trinucleotides are analyzed in a template-dependent polymerization assay. The specification discloses that "the dinucleotide is incorporated much better than the trinucleotide". However, there is no disclosure evaluating the incorporating of a tetranucleotide or pentanucleotide or hexanucleotide or octanucleotide in any combination or etc in an extension assay as claimed. Therefore, as to the quantity of experimentation required, one of skill in the art would have to design an experimental method commensurate in scope with the instant invention.

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II. *Amount of Direction and Guidance and Presence and Absence of Working Examples:*

The specification does not clearly provide any method that bears a reasonable correlation to the entire scope of the claims. The examples beginning at page 29 discloses methods of isolating five dinucleotide triphosphates (thymidylyl-3'-5'thymidine; deoxycytidylyl (3'-5')-2'-deoxyadenosine; deoxycytidylyl (3'-5')-2'-deoxycytidine; deoxyadenylyl (3'-5')-2'-deoxyguanosine; thymidylyl (3'-5')-2'-deoxycytidine) and one trinucleotide triphosphate (thymidylyl-3'-5'thymidylyl-3'-5'-thymidine). However, there is no direction or guidance given for incorporating or obtaining 4^N oligonucleotide triphosphates, each including N monomers, wherein N is any integer greater than 1, besides the dinucleotides and trinucleotide mentioned above. Therefore, further experimentation is required to one of skill in the art.

III. *Nature of the Invention*

The nature of the invention is incorporating of 4^N oligonucleotide triphosphates, each including N monomers, wherein N is an integer greater than 1. However, Applicant has only shown the incorporation of several dinucleotides and one trinucleotide. Therefore, the method of incorporating other oligonucleotide triphosphates is not reproducible due to the lack of guidance presented in the specification. As noted earlier, the specification does not properly disclose a method of making or using the claimed invention that bears a reasonable correlation to the entire scope of the claim.

IV. *Relative skill of those in the art and predictability or unpredictability of the art*

The level of skill in the art at the time the invention was made is very high. However, the level of unpredictability in the art is also high. For example, Moroney et al ((Biochemistry, vol. 30, No. 42, page 10438, col. 2, second full paragraph, lines 43-47) teach that "the incorporation

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of dinucleotide and trinucleotides into the product represents the limit of tolerance for the polymerase, and longer oligonucleotides, although complementary to the template strand, cannot be incorporated as initiating nucleotides". Likewise, the specification substantiates the level of unpredictability in the art in the teaching that dinucleotides incorporate better than the trinucleotide in the extension assay (Example 7) and lack of teaching of any other incorporation of oligonucleotide triphosphates. Therefore, for all of the foregoing reasons, undue experimentation is necessary for one of skill in the art to obtain the invention as claimed.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 12 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Moroney et al (Biochemistry, vol. 30, No. 42, pages 10343-49, 1991). Regarding claim 12, Moroney et al teach a method for extending a nascent oligonucleotide-3-OH in template dependent manner, the method comprising the step of contacting the nascent oligonucleotide-3-OH with a nucleic acid template, a template dependent polymerase and at least one oligonucleotide triphosphate under conditions in which said nascent oligonucleotide 3-OH hybridizes with said nucleic acid template and said template dependent polymerase is active in incorporating said at least one oligonucleotide triphosphate onto a growing 3' OH group of the nascent oligonucleotide-3-OH, thereby extending the nascent oligonucleotide 3'-OH in a template dependent manner (page 10347, col. 2, lines 4-10, 45-60).

Regarding claim 19, Moroney et al teach a method of extending a nascent oligonucleotide-3'-OH in a template dependent manner, the method comprising the step of contacting the nascent oligonucleotide 3'-OH with a nucleic acid template, a template dependent polymerase, at least one oligonucleotide triphosphate and at least one nucleotide triphosphate, wherein said at least one oligonucleotide triphosphate and said at least one nucleotide triphosphate are selected such that at least one monomer of said at least one oligonucleotide triphosphate is absent from said at least one nucleotide triphosphate under conditions under which said nascent oligonucleotide 3'-OH hybridizes with said nucleic acid template and said template-dependent polymerase is active in incorporating said at least one oligonucleotide triphosphate onto a growing 3'-OH of the nascent oligonucleotide 3'-OH, thereby extending the nascent oligonucleotide 3'-OH in a template dependent manner (page 10347, col. 2, lines 4-10, and 45-60). Therefore, Moroney et al meet the limitations of claims 12 and 19 of the instant invention.

Conclusion

6. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

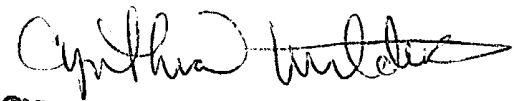
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.


CYNTHIA WILDER
PATENT EXAMINER
7/29/2004